REMARKS

I. Status of the Application

Claims 46-55, 61-76, 85, 86 and 90-92 are presently pending in the instant application. Claims 46-55, 62-71, 73-76, 85, 86 and 90-92 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Simone (U.S. Patent No. 5,397,786) in view of Thomas et al. (U.S. Patent No. 5,972,985, hereinafter "Thomas"), Buchholz et al. (U.S. Patent No. 6,514,973, hereinafter "Buchholz"), and Hageman et al. (U.S. Patent No. 6,420,342, hereinafter "Hageman"). Claim 72 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Simone in view of Thomas, Buchholz, and Kampinga et al. (U.S. Patent No. 6,455,511, hereinafter "Kampinga"), and further in view of Kuznicki et al. (U.S. Patent No. 5,464,619, hereinafter "Kuznicki"). Applicants respectfully request entry and consideration of the following remarks, which are intended to place the case in condition for allowance.

II. Disqualification of Hageman as Prior Art under 35 U.S.C. § 103(c)

Hageman is only available as prior art to the present application under 35 U.S.C. § 102(e). The present application (USSN 10/697,428) and Hageman (USPN 6,420,342) were, at the time the invention of USSN 10/697,428 was made, both owned by N.V. Nutricia of Zoetermeer, NL. Therefore, Applicants respectfully submit that Hageman should be disqualified as prior art under 35 U.S.C. § 103(c), and should not be cited as partial basis for the following 35 U.S.C. § 103(a) rejection.

III. Claims 46-55, 62-71, 73-76, 85-86, and 90-92 Are Not Obvious over Simone, Thomas, Buchholz, and Hageman

At page 3, section 4 of the instant Office Action, claims 46-55, 62-71, 73-76, 85, 86 and 90-92 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Simone in view of Thomas, Buchholz, and Hageman. Applicants respectfully traverse the rejection. As submitted above, Hageman should be disqualified as prior art. The combination of remaining cited references fails to render obvious Applicants' claimed invention.

The Examiner maintains that sarcosine and dimethylglycine are art-recognized equivalents to betaine at the time the invention was made, so one of ordinary skill in the art would have found it obvious to substitute sarcosine or dimethylglycine for betaine in the claimed fluid. The Examiner points to evidence from Buchholz and page 9, lines 18-20 of the instant specification. Applicants respectfully disagree.

> "In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and **cannot be based on applicant's disclosure** or the mere fact that the components at issue are functional or mechanical equivalents." (MPEP § 2144.06, emphasis added.)

Since Applicants' disclosure cannot be used as prior art against Applicants' claims, it is improper to use the specification to support the equivalency between betaine, diemethylglycine, and sarcosine. Moreover, Applicants' disclosure of the three compounds in a list of methylamines suitable for use in certain embodiments of Applicants' invention is not an admission of equivalence.

> "[T]here is a basic difference between (a) a showing by an application for patent of what the *art knows* to be equivalents or what means taken from the art he can use indiscriminately without affecting his invention in carry it out, and (b), a showing that *he has found*, as a part of his discovery or inventive process, that certain things may be used to achieve the same result. These findings are his property and he does not lose *all* of them just because of his

showing when it turns out that others have earlier discovered one or more of them." (*In re Ruff*, 256 F.2d 590, 118 USPQ 340, 346 (CCPA 1958.)

Additionally, just because betaine, dimethylglycine, and sarcosine are listed together as methyl donors in Buchholz does not imply that the three compounds are equivalent, much less that the three compounds can have equivalent function as osmolytes in a fluid for treating hypohydration. The skilled artisan looking for osmolytes to include in a fluid for treating hypohydration would not look to the methyl donors disclosed by Simone and Buchholz, because the skilled artisan would not expect any correlation between the property of being a methyl donor and the property of being an osmolyte. It is not the role of methyl donor that renders sarcosine and dimethylglycine particularly suitable for use in the present invention. Instead, it is their ability to act as osmolytes that renders them useful in a fluid that treats hypohydration.

Moreover, not all osmolytes are functionally equivalent in a fluid that treats hypohydration. As submitted in the supplemental response filed on August 1, 2006, test results show that dimethylglycine and sarcosine have a strong beneficial effect on the viability of mammalian cells under dehydrated conditions, whereas several other organic osmolytes are not effective at all, or show a lesser beneficial effect. As discussed at pages 8-9 of the prior Office Action response filed on December 18, 2006, and incorporated herein by reference, dimethylglycine and sarcosine have different physical, chemical, and biological properties from betaine. Thus, the skilled artisan would not expect equivalent osmolytic function between betaine and dimethylglycine/sarcosine.

The Examiner is of the opinion that it would have been apparent to those skilled in the art to optimize amounts of known active and inactive ingredients to arrive at the range of methyl amine recited in claim 46. But it is not routine dosage determination if the function of the methyl donors disclosed by Simone and Buchholz is different from the function of the dimethylglycine and/or

sarcosine osmolyte in the claimed fluid. The optimal dosage amount for a methyl donor is not necessarily the same as, and may in fact be quite different from, the optimal dosage amount for an osmolyte in a fluid for treating hypohydration. This is in fact the case, as evidenced by the three orders of magnitude difference in the concentration of methyl donor disclosed by Simone in its rehydration drink and the low end of the concentration range of dimethylglycine and/or sarcosine osmolyte recited in the subject claims. [Simone discloses only 1-25 μg of betaine chloride per serving unit (Table 1). Simone discloses at column 6, lines 50-52 that 1 cup is 1 serving unit. Therefore, the maximum betaine chloride concentration disclosed by Simone is 25 μg per cup, which equals 0.000106 g/L. This amount, 0.000106 g/L, is three orders of magnitude smaller than the low end of the recited range for methyl amine in independent claim 46 (0.2 – 10 g/L).] Therefore, it is not routine experimentation to obtain the recited range of methyl amine osmolytes from the disclosed range of methyl donors in Simone, so the recited range is not obvious from the prior art.

The Examiner also cites US patents 6,514,973, 5,580,856, 6,020,139, 5,389,383 and US publication 2004/0192615, as disclosing betaine, sarcosine, and dimethylglycine as known methyl donors or osmoprotectant compounds. First of all, US publication 2004/0192615 has a priority date more than two years later than the priority date of the present application, so it should not be used as evidence of what was known in the art at the time the claimed invention was made. As discussed above, disclosure of compounds as methyl donors does not imply functional equivalence of those compounds as osmolytes. None of the citations that list all three of betaine, sarcosine, and dimethylglycine as osmolytes or osmoprotectants are drawn to the same technical field as Applicants' claimed invention (constituted with same ingredients and share common utilities), nor are they directed to the same problem which Applicants are concerned about. US 5,580,856 is directed to a reconstitution solution for dried protein having osmolytes suitable for increasing the

melting temperature of proteins (column 4, lines 30-47), and is not concerned with rehydration of cells, much less treating hypohydration in a complex multi-cellular organism. US 5,389,383 is directed to a solution for treating hypoxia-related ocular complications in contact lens wearers, where osmoprotectants are included to reduce swelling and reduce the elevated hydration of the cornea (column 4, lines 30-44). This is completely opposite to Applicants' use of osmolytes to increase water intake by the cells of a subject suffering from hypohydration. Therefore, the cited references are not analogous to Applicants' claimed invention, and should not be used as basis for prior art functional equivalence of betaine and dimethylglycine and sarcosine as osmolytes.

For at least the foregoing reasons, dimethylglycine and sarcosine are not art-recognized functional (osmolyte) equivalents of betaine, so the skilled artisan would not find it obvious to substitute dimethylglycine or sarcosine for betaine in a fluid that treats hypohydration.

Regarding the claim limitation of osmolarity between 70 and 275 mOsm/L, the Examiner maintains that differences in concentration will not support patentability unless there is evidence indicating criticality of the recited concentration. The Examiner is of the opinion that when general conditions are disclosed in the prior art, it is not inventive to discover the optimum or workable concentration ranges by routine experimentation. In previous Office Action responses, Applicants have distinguished the subject claims, which recite hypotonic osmolarities between 70 and 275 mOsm/L, from the citations over which the claims have been rejected, which disclose hypertonic solutions. Applicants respectfully submit that the change in concentration of osmolytes between a hypertonic solution and a hypotonic solution is not just a difference in degree, as the Examiner asserts, but a **difference in kind**. A hypotonic solution is defined in the art as having a lower concentration of solutes than the cytoplasm of a cell. So when a cell is placed in a hypotonic solution, osmotic pressure causes a net flow of water into the cell. In contrast, a hypertonic solution

is defined in the art as having a higher concentration of solutes than the cytoplasm of a cell. So when a cell is placed in a hypertonic solution, osmotic pressure causes a net flow of water out of the cell into the solution. Thus, hypotonic solutions have a **completely opposite osmotic property** from hypertonic solutions. The decrease in solute concentration from hypertonic to hypotonic solution does not lead to a proportional and linear change in osmotic property. Instead, a decrease in solute concentration leads to a decrease in the net amount of water moving out of a cell as the solution becomes less hypertonic, until an equilibrium point is reached at the isotonic concentration, and then continued decrease of solute concentration leads to a complete reversal of osmotic property where water increasingly moves into a cell as the solution becomes more hypotonic. Thus, it would not be an obvious optimization of solute concentration to decrease the concentration from hypertonic to hypotonic solution.

The skilled artisan looking to optimize the hypertonic solutions disclosed in, for example, Simone, would increase the hypertonicity of the solution by increasing the amount of the disclosed active ingredients, about 30 different macronutrients and micronutrients, since Simone teaches that truly spectacular results are obtained from its hypertonic rehydration drinks (column 5, lines 26-31, Table 1). The skilled artisan would not be motivated to decrease the active ingredients so much that the solution becomes hypotonic, since Simone teaches that hypertonic solutions having many active ingredients give good results. Applicants' claimed invention uses a completely different mechanism to increase water absorption in a subject suffering from hypohydration. Instead of including a high concentration of many different types of active ingredients, Applicants' claimed fluid uses osmotic pressure from a hypotonic solution (one having a low concentration of solutes, lower than the solute concentration in a cell) to push water into cells. Thus, the hypotonic osmolarity in the range of 70 to

275 mOsm/L recited in the subject claims is critical for Applicants' fluid to function as a treatment for hypohydration.

Regarding the combination of dimethylglycine and/or sarcosine and a hypotonic fluid, the presence of dimethylglycine and/or sarcosine in a hypotonic fluid of the invention slows down the process of cell-shrinkage as a result of hypohydration. Cell-shrinkage has a negative effect on the functioning of proteins and/or other intracellular components. In a shrunken cell, ion and protein concentrations are abnormally increased, which negatively affects cell processes, e.g., protein folding and enzyme functions. Such negative effects are reduced by the slowing down of cell shrinkage. The hypotonic property of a fluid of the invention is beneficial to stimulate cell swelling by pushing water into the cells of hypohydrated subjects, so that shrunken cells swell back to normal proportions. Thus, the combination of a hypotonic fluid with dimethylglycine and/or sarcosine is beneficial to restore and maintain normal cell size. Such a combination is not taught or suggested by the cited references.

As discussed in previous Office Action responses filed on July 18, 2006, August 1, 2006, December 18, 2006, and March 16, 2007 and incorporated herein by reference, the combination of Simone, Thomas, and Buchholz fails to teach or suggest or provide motivation for a fluid for treating hypohydration comprising dimethylglycine or sarcosine and having an essentially hypotonic osmolarity in the range of 70 to 275 mOsm/L, as recited in the subject claims. For at least the reasons discussed above, the claimed subject matter does not plainly or logically follow from the cited references. Therefore, the cited references, alone or in combination, fail to render the claimed invention obvious. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejection and allowance of claims 46-55, 62-71, 73-76, 85, 86 and 90-92 under be reconsidered and withdrawn.

IV. Claim 72 Is Not Obvious over Simone in View of Thomas, Buchholz, Kampinga, and further in View of Kuznicki

At page 7, section 5 of the instant Office Action, claim 72 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Simone in view of Thomas, Buchholz, Kampinga, and further in view of Kuznicki. Applicants respectfully traverse the rejection. As discussed in section III above, the combination of Simone, Thomas, and Buchholz fails to render obvious a fluid for treating hypohydration comprising dimethylglycine or sarcosine and having an essentially hypotonic osmolarity in the range of 70 to 275 mOsm/L, as recited in the subject claims. Kampinga and Kuznicki fail to remedy the deficiencies of Simone, Thomas, and Buchholz. Neither Kampinga nor Kuznicki teach or suggest or provide motivation for a fluid for treating hypohydration that is both hypotonic with an osmolarity from 70 to 275 mOsm/L and comprises dimethylglycine and/or sarcosine.

Thus, the combination of Simone Thomas, Buchholz, Kampinga, and Kuznicki fails to render claim 72 obvious. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejection and allowance of claim 72.

V. Conclusion

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 720-9600. The Commissioner is hereby authorized to charge any additional fees or credit overpayment to Deposit Account No. 19-0733.

Respectfully submitted,

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